



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-16,32-34

Methods of synthesis of peptides comprising the step of linking the auxiliary compound of formula I to an amine nitrogen atoms to facilitate conversion of the amine (i.e. the same amine that has been linked to the auxiliary compound) to amide; auxiliary compounds and kits thereof.

2. Claims: 17-21

Methods of synthesis of cyclic peptides comprising the step of linking the auxiliary compound to a primary amine of the corresponding linear peptides.

3. Claims: 22-23

Methods of synthesis of "large" peptides comprising the step of linking the auxiliary compound to a primary amine of a peptide fragment.

4. Claims: 24-25

Methods of synthesis of "difficult" peptides comprising the step of linking the auxiliary compound to one or more nitrogen atoms of a peptide linked to a solid support.

5. Claims: 26-31

Methods of solid phase synthesis of peptides comprising the step of using the auxiliary compound as a linker that binds the alpha-nitrogen of an amino acid residue to the solid support.

1) The common concept, which would link the subject-matter of the above mentioned groups of claims, is the idea of linking the auxiliary compound to nitrogen atoms in peptide synthesis (the nitrogen atoms are specifically amine nitrogen atoms when subjects 1, 2, 3 and 5 are considered).

2) This concept is not new for the following reason.

a) Document "EP 0091330" discloses (see examples 1 and 9) a peptide synthesis, which comprises the step of linking 2-hydroxy-5-nitro-benzaldehyde to the N-terminal nitrogen atom of aspartic acid. The 2-hydroxy-5-nitro-benzaldehyde is an auxiliary compounds according to the definitions of claim 1.

b) In the synthetic methods disclosed in "US 3704246" activated/protected amino acid residues are reacted with amino acid esters to form the desired peptides (see column 1, lines 60-67). Said activated/protected residues are obtained by linking halo- or nitro-salicylaldehydes to the N-terminal ends of amino acids (see column 3, lines 60-67). The methods disclosed in this document therefore comprise the step of linking compounds, i.e. auxiliary compounds



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according to the definitions of claim 1, to amine nitrogen atoms.

3) With respect to the fact that the conversion of the amine (which has been linked to the auxiliary compound) to amide is not a feature of the methods defined by claims 17-21, 22-23, 24-25 and 26-31.

No technical relationship, to which an inventive step can be addressed, is present among the subjects defined by the claims of each group above and a lack of Unity "a posteriori" is indicated (Art. 82 EPC).



**under Rule 46, paragraph 1 of the European Patent EP 99 95 0390 Convention**

**Application Number**5



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	PASHAYAN A.A. ET AL.: "Photorearrangement of o-nitrobenzaldehyde and its derivatives" KHIM. VYS. ENERG., vol. 10, no. 2, 1976, pages 155-160, XP001094469 * table 2 *	34	
X	US 5 539 138 A (FLANAGAN RICHARD J ET AL) 23 July 1996 (1996-07-23) * column 5, line 43 - column 6, line 55 *	34	
D,Y	HYDE C ET AL: "SOME 'DIFFICULT SEQUENCES' MADE EASY A STUDY OF INTERCHAIN ASSOCIATION IN SOLID-PHASE PEPTIDE SYNTHESIS" INTERNATIONAL JOURNAL OF PEPTIDE AND PROTEIN RESEARCH, MUNKSGAARD, COPENHAGEN, DK, vol. 43, no. 5, 1 May 1994 (1994-05-01), pages 431-440, XP000440865 ISSN: 0367-8377 * reaction scheme on page 432, left-hand column *	1-3,6-8, 13,14, 16,34	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Y	JOHNSON ET AL: "N,O-bisFmoc derivatives of N-(2-hydroxy-4-methoxybenzyl)-amino acids: useful intermediates in peptide synthesis" JOURNAL OF PEPTIDE SCIENCE, JOHN WILEY AND SONS LTD, GB, vol. 1, 1995, pages 11-25, XP002141383 ISSN: 1075-2617 * page 15, paragraph joining left- and right-hand columns; page 16, left-hand column, lines 2-5; page 20, left-hand column, 3rd paragraph; table 7 *	1-3,6-8, 13,14, 16,34	

**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 99 95 0390

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on  
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20-08-2002

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
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			IT	1194171 B	14-09-1988
			LU	84733 A1	17-11-1983
			PT	76514 A ,B	01-05-1983
US 3704246	A	28-11-1972	GB	1348512 A	20-03-1974
US 5539138	A	23-07-1996	CA	2154214 A1	28-01-1996